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US Filed on

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(71) Applicants (for all designated States except US): IN-CYTE GENOMICS, INC. [US/US]; 3160 Porter Drive, Palo Alto, CA 94304 (US). BAUGHN, Mariah, R. [US/US]; 14244 Santiago Road, San Leandro, CA 94577 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): BANDMAN, Olga [US/US]; 366 Anna Avenue, Mountain View, CA 94043 (US). YUE, Henry [US/US]; 826 Lois Avenue, Sunnyvale, CA 94087 (US). LAL, Preeti [IN/US]; 2382 Lass Drive, Santa Clara, CA 95054 (US). TANG, Y., Tom [CN/US]; 4230 Ranwick Court, San Jose, CA 95118 (US). **REDDY, Roopa** [IN/US]; 1233 W. McKinley Avenue #3, Sunnyvale, CA 94086 (US). **AZIMZAI, Yalda** [US/US]; 2045 Rock Springs Drive, Hayward, CA 94545 (US).

- (74) Agents: HAMLET-COX, Diana et al.; Incyte Genomics, Inc., 3160 Porter Drive, Palo Alto, CA 94304 (US).
- (81) Designated States (national): AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW.
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78952 /

(54) Title: HUMAN RNA METABOLISM PROTEINS (RMEP)

(57) Abstract: The invention provides human RNA metabolism proteins (RMEP) and polynucleotides which identify and encode RMEP. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating, or preventing disorders associated with expression of RMEP.



SEQUENCE LISTING

<110> INCYTE GENOMICS, INC.
BANDMAN, Olga
YUE, Henry
LAL, Preeti
TANG, Y. Tom
REDDY, Roopa
BAUGHN, Mariah R.
AZIMZAI, Yalda

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<151> 1999-06-17

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Cys Arg Thr His Leu Gly His Leu Leu Asn Pro Gly Asp Leu Val
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				95		His			100					Thr
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				155		Leu			160					165
				170		Leu			175					180
				185		Ala			190					195
				200		Ile			205					210
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				395		Pro			400			-		405
				410		His			415					420
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				440		Pro			445					450
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Arg Pro Ala Arg Thr Pro Pro Arg Arg Thr Leu Ser Gly Ser
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Gly Ser Gly Ser Gly Ser Tyr Ser Gly Ser Ser Ser Arg Ser
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Ala Asp Leu Ala Ser Pro Val Ser Ser Ala Ser Ser Arg Ser Pro
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                                    295
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Pro Pro Lys Ser Ala Lys Pro Pro Ala Gly Gly Lys Ser Ser Gln
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Gln Pro Ser Thr Pro Gln Gln Ala Pro Pro Gly Gln Pro Gln Gln
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Gly Tyr Gly Pro Glu Ser Glu Leu Ser Gln Ala Ser Ala Ala Thr
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Lys Met Lys Asp Pro Lys Gln Ile Ile Arg Asp Met Glu Lys Leu
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                                     55
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                                     70
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Val Glu Ser Ile Pro Leu Pro Asp Met Pro His Ala Pro Ser Asn
                140
                                    145
Ile Leu Ile Gln Asp Ile Pro Leu Pro Gly Ala Gln Pro Pro Ser
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                                    160
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Ile Leu Lys Lys Thr Ser Ala Tyr Gly Pro Pro Thr Arg Ala Val
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                                    175
                                                         180
Ser Ile Leu Pro Leu Leu Gly His Gly Val Pro Arg Leu Pro Pro
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                                    190
                                                         195
Gly Arg Lys Pro Pro Gly Pro Pro Pro Pro Pro Pro Pro Pro Gln
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                                    205
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Val Val Gln Met Tyr Gly Arg Lys Val Gly Phe Ala Leu Asp Leu
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                                    220
Pro Pro Arg Arg Arg Asp Glu Asp Met Leu Tyr Ser Pro Glu Leu
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                                    235
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                                    250
Asp Gly Tyr Pro Glu Asp Met Asp Gln Asp Lys His Asp Asp Ser
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				Leu 335					340					345
				Glu 350					355					360
			•	Glu 365					370					375
				Ser 380					385					390
				Gln 395					400					405
				Pro 410					415					420
				Gly 425					430					435
				Pro 440					445					450
				Pro 455					460					465
				Pro 470					475					480
				Arg 485					490					495
				Pro 500					505					510
				Leu 515					520					525
				Asn 530					535	Ala	Pro	Pro	Asn	Leu 540
				Lys 545					550		Ala			555
				Ala 560					565					570
				Ile 575					580					585
				Lys 590					595					600
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Ile Asp Ile Phe Thr Gly Lys Lys Tyr Glu Asp Ile Cys Pro Ser
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                                      40
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Lys Gln Lys Val Glu Gln Asn Ala Ala Pro Ser His Thr Lys Phe
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                                      55
                                                          60
Ser Ile Tyr Pro Pro Ile Pro Gly Glu Glu Ser Ser Leu Arg Trp
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                                      70
Ala Gly Lys Lys Phe Glu Glu Ile Pro Ile Ala His Ile Lys Ala
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                                      85
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Ser His Asn Asn Thr Gln Ile Gln Val Val Ser Ala Ser Asn Glu
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                                     100
Pro Leu Ala Phe Ala Ser Cys Gly Thr Glu Gly Phe Arg Asn Ala
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                                     115
Lys Lys Gly Thr Gly Ile Ala Ala Gln Thr Ala Gly Ile Ala Ala
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Thr Tyr Arg Thr Ser Met Phe Lys Thr Phe Lys Lys Thr Leu Asp
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Asp Gly Phe Phe Pro Phe Ile Ile Leu Asp Ala Ile Asn Asp Arg
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Gly	Gly	Asp	Ile	Cys 200	Gln	Gln	Phe	Thr	Arg 205	Glu	Ile	Phe	Asp	Met 210
Tyr	Gln	Asn	Tyr	Ser 215	Суѕ	Tyr	Lys	His	Trp 220	Gln	Phe	Glu	Leu	Leu 225
Asn	Tyr	Thr	Pro	Ala 230	Asp	Tyr	Gly	Gly	Leu 235	His	His	Ala	Ala	Ala 240
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Gly	Ile	His	Arg	Val 260	Gln	Arg	Ile	Pro	Glu 265	Val	Gly	Leu	Ser	Ser 270
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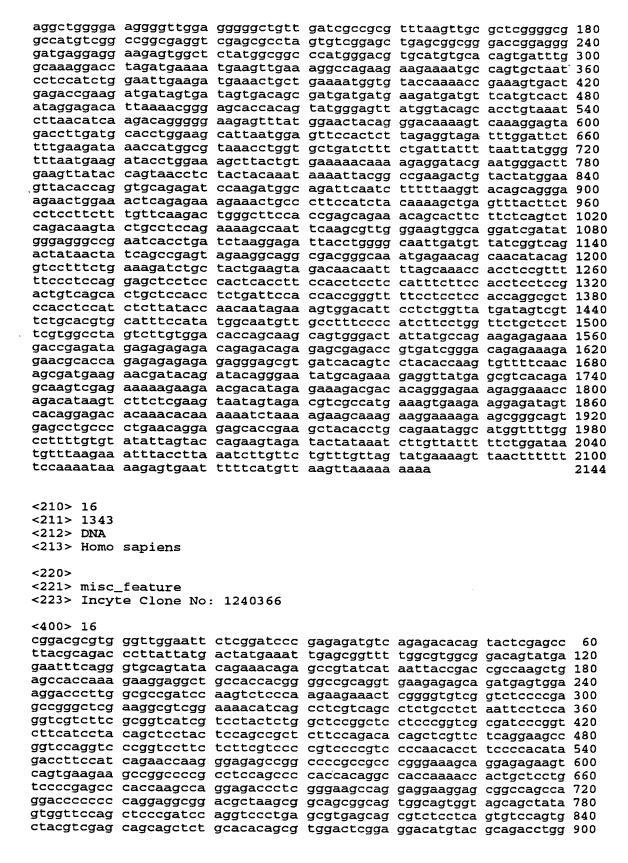
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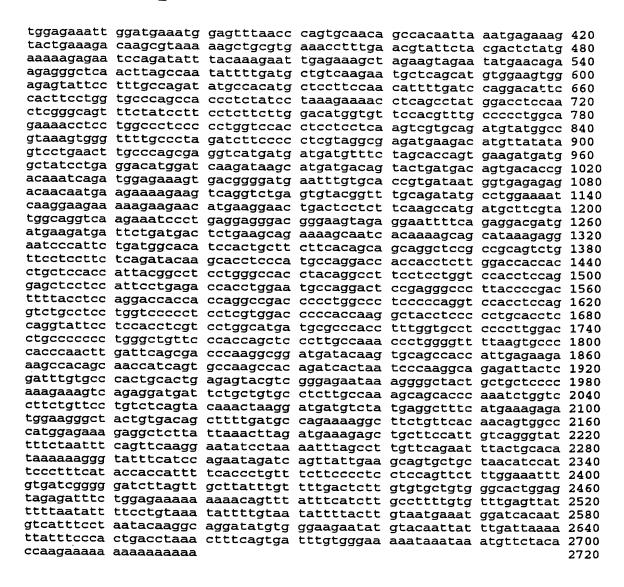
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INTERNATIONAL SEARCH REPORT

*ional Application No Ci/US 00/16644

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12N15/12 C12N5/10 C12Q1/68

C07K16/18

C07K14/47 A61K38/00 C12N15/00

A01K67/027

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

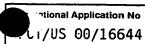
STRAND, EPO-Internal, WPI Data, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT						
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.				
Α	WILSON R ET AL: "2.2 MB OF CONTIGUOUS NUCLEOTIDE SEQUENCE FROM CHROMOSOME III OF C. ELEGANS" NATURE,GB,MACMILLAN JOURNALS LTD. LONDON, vol. 368, no. 6466, 3 March 1994 (1994-03-03), pages 32-38, XP002029739 ISSN: 0028-0836 the whole document	1				
Α	WO 98 23744 A (INCYTE PHARMA INC ;BANDMAN OLGA (US); GOLI SURYA K (US)) 4 June 1998 (1998-06-04) the whole document	1				

Further documents are listed in the continuation of box C.	X Patent family members are listed in annex.					
"A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention invention. "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone. "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family					
Date of the actual completion of the international search 17 January 2001	Date of mailing of the international search report 2 5. 04. 2001					
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer CHAMBONNET, F					

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INTERNATIONAL SEARCH REPORT



0.10	- No. O. O. C.					
	ation) DOCUMENTS CONSIDERED TO BE RELEVANT					
Category °	Citation of document, with indication where appropriate, of the relevant passages	Relevant to claim No.				
Ρ,Χ	EMBL ACCESSION NUMBER Q9Y2Z6; SEQUENCE CHARACTERISATION CGI-07 PROTEIN. Homo sapiens (Human). DT 01-NOV-1999 (TrEMBLrel. 12, Created) Lin WC.; "Comparative gene cloning: Identification of novel human genes with C. elegans proteome as template."; XP002157664 the whole document	1				

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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
see additional sheet
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: see further information sheet invention group1.
Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: partially 1-27

An isolated polypeptide comprising an amino acid sequence selected from the group consisting of: a) an amino acid sequence consisting of SEQ ID NO:1, b) a naturally occurring amino acid sequence having at least 90% sequence identity to SEQ ID NO:1, c) a biologically active fragment of an amino acid sequence consisting in SEQ ID NO:1, d) an immunogenic fragment of an amino acid sequence consisting in SEQ ID NO:1; an isolated polynucleotide encoding said polypeptide or consisting of SEQ ID NO:14; a cell transformed with such a recombinant polynucleotide; a transgenic organism comprising said recombinant polynucleotide; an isolated antibody which specifically bins to said polypeptide; an hybridization method for detecting a target said polynucleotide; a pharmaceutical composition comprising an effective amount of said polypeptide and a pharmaceutically acceptable excipient; methods for screening agonists, antagonists, binding compounds , of said polypeptide and pharmaceutical compositions comprising an effective amount thereof and a pharmaceutically acceptable excipient; method for treating a disease or condition associated with an altered expression of said functional polypeptide using said pharmaceutical compositions:

2. Claims: partially 1-27

An isolated polypeptide comprising an amino acid sequence selected from the group consisting of: a) an amino acid sequence consisting of SEQ ID NO:2, b) a naturally occuring amino acid sequence having at least 90% sequence identity to SEQ ID NO:2, c) a biologically active fragment of an amino acid sequence consisting in SEQ ID NO:2, d) an immunogenic fragment of an amino acid sequence consisting in SEQ ID NO:2; an isolated polynucleotide encoding said polypeptide or consisting of SEQ ID NO:15; a cell transformed with such a recombinant polynucleotide; a transgenic organism comprising said recombinant polynucleotide; an isolated antibody which specifically bins to said polypeptide; an hybridization method for detecting a target said polynucleotide; a pharmaceutical composition comprising an effective amount of said polypeptide and a pharmaceutically acceptable excipient; methods for screening agonists, antagonists, binding compounds, of said polypeptide and pharmaceutical compositions comprising an effective amount thereof and a pharmaceutically acceptable excipient; method for treating a disease or condition associated with an altered expression of said functional polypeptide using said pharmaceutical compositions:

3. Claims: partially 1-27

An isolated polypeptide comprising an amino acid sequence selected from the group consisting of: a) an amino acid sequence consisting of SEQ ID NO:3, b) a naturally occuring amino acid sequence having at least 90% sequence identity to SEQ ID NO:3, c) a biologically active fragment of an amino acid sequence consisting in SEQ ID NO:3, d) an immunogenic fragment of an amino acid sequence consisting in SEQ ID NO:3;an isolated polynucleotide encoding said polypeptide or consisting of SEQ ID NO:16; a cell transformed with such a recombinant polynucleotide; a transgenic organism comprising said recombinant polynucleotide; an isolated antibody which specifically bins to said polypeptide; an hybridization method for detecting a target said polynucleotide; a pharmaceutical composition comprising an effective amount of said polypeptide and a pharmaceutically acceptable excipient; methods for screening agonists, antagonists, binding compounds polypeptide and pharmaceutical compositions comprising an effective amount thereof and a pharmaceutically acceptable excipient; method for treating a disease or condition associated with an altered expression of said functional polypeptide using said pharmaceutical compositions:

4. Claims: partially 1-27

An isolated polypeptide comprising an amino acid sequence selected from the group consisting of: a) an amino acid sequence consisting of SEQ ID NO:4, b) a naturally occuring amino acid sequence having at least 90% sequence identity to SEQ ID NO:4. c) a biologically active fragment of an amino acid sequence consisting in SEQ ID NO:4. d) an immunogenic fragment of an amino acid sequence consisting in SEQ ID NO:4; an isolated polynucleotide encoding said polypeptide or consisting of SEQ ID NO:17; a cell transformed with such a recombinant polynucleotide; a transgenic organism comprising said recombinant polynucleotide; an isolated antibody which specifically bins to said polypeptide; an hybridization method for detecting a target said polynucleotide; a pharmaceutical composition comprising an effective amount of said polypeptide and a pharmaceutically acceptable excipient; methods for screening agonists, antagonists, binding compounds, of said polypeptide and pharmaceutical compositions comprising an effective amount thereof and a pharmaceutically acceptable excipient; method for treating a disease or condition associated with an altered expression of said functional polypeptide using said pharmaceutical compositions;

5. Claims: partially 1-27

An isolated polypeptide comprising an amino acid sequence selected from the group consisting of: a) an amino acid sequence consisting of SEQ ID NO:5, b) a naturally occuring amino acid sequence having at least 90% sequence identity to SEQ ID NO:5, c) a biologically active fragment of an amino acid sequence consisting in SEQ ID NO:5. d) an immunogenic fragment of an amino acid sequence consisting in SEQ ID NO:5; an isolated polynucleotide encoding said polypeptide or consisting of SEQ ID NO:18; a cell transformed with such a recombinant polynucleotide; a transgenic organism comprising said recombinant polynucleotide; an isolated antibody which specifically bins to said polypeptide; an hybridization method for detecting a target said polynucleotide; a pharmaceutical composition comprising an effective amount of said polypeptide and a pharmaceutically acceptable excipient; methods for screening agonists, antagonists, binding compounds, of said polypeptide and pharmaceutical compositions comprising an effective amount thereof and a pharmaceutically acceptable excipient; method for treating a disease or condition associated with an altered expression of said functional polypeptide using said pharmaceutical compositions:

6. Claims: partially 1-27

An isolated polypeptide comprising an amino acid sequence selected from the group consisting of: a) an amino acid sequence consisting of SEQ ID NO:6, b) a naturally occuring amino acid sequence having at least 90% sequence identity to SEQ ID NO:6, c) a biologically active fragment of an amino acid sequence consisting in SEQ ID NO:6, d) an immunogenic fragment of an amino acid sequence consisting in SEQ ID NO:6; an isolated polynucleotide encoding said polypeptide or consisting of SEQ ID NO:19; a cell transformed with such a recombinant polynucleotide; a transgenic organism comprising said recombinant polynucleotide; an isolated antibody which specifically bins to said polypeptide; an hybridization method for detecting a target said polynucleotide; a pharmaceutical composition comprising an effective amount of said polypeptide and a pharmaceutically acceptable excipient; methods for screening agonists, antagonists, binding compounds , of said polypeptide and pharmaceutical compositions comprising an effective amount thereof and a pharmaceutically acceptable excipient; method for treating a disease or condition associated with an altered expression of said functional polypeptide using said pharmaceutical compositions;

7. Claims: partially 1-27

An isolated polypeptide comprising an amino acid sequence selected from the group consisting of: a) an amino acid sequence consisting of SEQ ID NO:1, b) a naturally occuring amino acid sequence having at least 90% sequence identity to SEQ ID NO:1, c) a biologically active fragment of an amino acid sequence consisting in SEQ ID NO:1, d) an immunogenic fragment of an amino acid sequence consisting in SEQ ID NO:1; an isolated polynucleotide encoding said polypeptide or consisting of SEQ ID NO:21; a cell transformed with such a recombinant polynucleotide; a transgenic organism comprising said recombinant polynucleotide; an isolated antibody which specifically bins to said polypeptide; an hybridization method for detecting a target said polynucleotide; a pharmaceutical composition comprising an effective amount of said polypeptide and a pharmaceutically acceptable excipient; methods for screening agonists, antagonists, binding compounds, of said polypeptide and pharmaceutical compositions comprising an effective amount thereof and a pharmaceutically acceptable excipient; method for treating a disease or condition associated with an altered expression of said functional polypeptide using said pharmaceutical compositions;

8. Claims: partially 1-27

An isolated polypeptide comprising an amino acid sequence selected from the group consisting of: a) an amino acid sequence consisting of SEQ ID NO:8, b) a naturally occuring amino acid sequence having at least 90% sequence identity to SEQ ID NO:8, c) a biologically active fragment of an amino acid sequence consisting in SEQ ID NO:8, d) an immunogenic fragment of an amino acid sequence consisting in SEQ ID NO:8; an isolated polynucleotide encoding said polypeptide or consisting of SEO ID NO:214; a cell transformed with such a recombinant polynucleotide; a transgenic organism comprising said recombinant polynucleotide; an isolated antibody which specifically bins to said polypeptide; an hybridization method for detecting a target said polynucleotide; a pharmaceutical composition comprising an effective amount of said polypeptide and a pharmaceutically acceptable excipient; methods for screening agonists, antagonists, binding compounds, of said polypeptide and pharmaceutical compositions comprising an effective amount thereof and a pharmaceutically acceptable excipient; method for treating a disease or condition associated with an altered expression of said functional polypeptide using said pharmaceutical compositions:

9. Claims: partially 1-27

An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

a) an amino acid sequence consisting of SEQ ID NO:9,

- b) a naturally occurring amino acid sequence having at least 90% sequence identity to SEQ ID NO:9,
- c) a biologically active fragment of an amino acid sequence consisting in SEQ ID NO:9,
- d) an immunogenic fragment of an amino acid sequence consisting in SEQ ID NO:9; an isolated polynucleotide encoding said polypeptide or consisting of SEQ ID NO:22; a cell transformed with such a recombinant polynucleotide; a transgenic organism comprising said recombinant polynucleotide; an isolated antibody which specifically bins to said polypeptide; an hybridization method for detecting a target said polynucleotide; a pharmaceutical composition comprising an effective amount of said polypeptide and a pharmaceutically acceptable excipient; methods for screening agonists, antagonists, binding compounds, of said polypeptide and pharmaceutical compositions comprising an effective amount thereof and a pharmaceutically acceptable excipient; method for treating a disease or condition associated with an altered expression of said functional polypeptide using said pharmaceutical compositions;

10. Claims: partially 1-27

An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

- a) an amino acid sequence consisting of SEQ ID NO:10,
- b) a naturally occuring amino acid sequence having at least 90% sequence identity to SEQ ID NO:10,
- c) a biologically active fragment of an amino acid sequence
- consisting in SEQ ID NO:10,
- d) an immunogenic fragment of an amino acid sequence consisting in SEQ ID NO:10; an isolated polynucleotide encoding said polypeptide or consisting of SEQ ID NO:23; a cell transformed with such a recombinant polynucleotide; a transgenic organism comprising said recombinant polynucleotide; an isolated antibody which specifically bins to said polypeptide; an hybridization method for detecting a target said polynucleotide; a pharmaceutical composition comprising an effective amount of said polypeptide and a pharmaceutically acceptable excipient; methods for screening agonists, antagonists, binding compounds, of said polypeptide and pharmaceutical compositions comprising an effective amount thereof and a pharmaceutically acceptable excipient: method for treating a disease or condition associated with an altered expression of said functional polypeptide using said pharmaceutical compositions;

11. Claims: partially 1-27

PCT/ISA/ 210 FURTHER INFORMATION CONTINUED FROM

An isolated polypeptide comprising an amino acid sequence selected from the group consisting of: a) an amino acid sequence consisting of SEQ ID NO:11, b) a naturally occuring amino acid sequence having at least 90% sequence identity to SEQ ID NO:11, c) a biologically active fragment of an amino acid sequence consisting in SEQ ID NO:11, d) an immunogenic fragment of an amino acid sequence consisting in SEQ ID NO:11; an isolated polynucleotide encoding said polypeptide or consisting of SEQ ID NO:24; a cell transformed with such a recombinant polynucleotide; a transgenic organism comprising said recombinant polynucleotide; an isolated antibody which specifically bins to said polypeptide; an hybridization method for detecting a target said polynucleotide; a pharmaceutical composition comprising an effective amount of said polypeptide and a pharmaceutically acceptable excipient; methods for screening agonists, antagonists, binding compounds, of said polypeptide and pharmaceutical compositions comprising an effective amount thereof and a pharmaceutically acceptable excipient; method for treating a disease or condition associated with an altered expression of said functional polypeptide using said pharmaceutical compositions;

12. Claims: partially 1-27

An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

a) an amino acid sequence consisting of SEQ ID NO:12,

b) a naturally occuring amino acid sequence having at least

90% sequence identity to SEQ ID NO:12, c) a biologically active fragment of an amino acid sequence

consisting in SEQ ID NO:12,

d) an immunogenic fragment of an amino acid sequence consisting in SEQ ID NO:12; an isolated polynucleotide encoding said polypeptide or consisting of SEQ ID NO:25; a cell transformed with such a recombinant polynucleotide: a transgenic organism comprising said recombinant polynucleotide; an isolated antibody which specifically bins to said polypeptide; an hybridization method for detecting a target said polynucleotide; a pharmaceutical composition comprising an effective amount of said polypeptide and a pharmaceutically acceptable excipient; methods for screening agonists, antagonists, binding compounds, of said polypeptide and pharmaceutical compositions comprising an effective amount thereof and a pharmaceutically acceptable excipient; method for treating a disease or condition associated with an altered expression of said functional polypeptide using said pharmaceutical compositions;

13. Claims: partially 1-27

An isolated polypeptide comprising an amino acid sequence

selected from the group consisting of: a) an amino acid sequence consisting of SEQ ID NO:13, b) a naturally occuring amino acid sequence having at least 90% sequence identity to SEQ ID NO:13, c) a biologically active fragment of an amino acid sequence consisting in SEQ ID NO:13, d) an immunogenic fragment of an amino acid sequence consisting in SEQ ID NO:13; an isolated polynucleotide encoding said polypeptide or consisting of SEQ ID NO:26; a cell transformed with such a recombinant polynucleotide; a transgenic organism comprising said recombinant polynucleotide; an isolated antibody which specifically bins to said polypeptide; an hybridization method for detecting a target said polynucleotide; a pharmaceutical composition comprising an effective amount of said polypeptide and a pharmaceutically acceptable excipient; methods for screening agonists, antagonists, binding compounds, of said polypeptide and pharmaceutical compositions comprising an effective amount thereof and a pharmaceutically acceptable excipient; method for treating a disease or condition associated with an altered expression of said functional

polypeptide using said pharmaceutical compositions;

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tion on patent family members

otional Application No I/US 00/16644

Patent document cited in search report	Publication date	Patent family member(s)	Publication date		
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